FOUNDATION FOR PRADER-WILLI RESEARCH

What’s Happening in PWS Research

Webinar transcript • November 17, 2026

Susan Hedstrom, Executive Director • Theresa Strong, PhD, Director of Research Programs

Edited from the YouTube captions for readability. Research and trial updates reflect what was shared during the webinar.

Introduction

Susan Hedstrom. Welcome, everyone, to today’s webinar, What’s Happening in PWS Research. I can give you a little sneak peek: it’s a lot. I’m Susan Hedstrom, the executive director of FPWR. Today you’ll hear from our director of research programs and co-founder, Dr. Theresa Strong. She’ll share highlights from PWS research and talk us through a few of the 18 research projects we recently funded. As always, we want to hear from you. Please use the Q&A feature to submit questions during the presentation. We’ll try to answer as many as we can at the end. With that, I’ll turn it over to Dr. Theresa Strong.

Theresa Strong, PhD. Thank you so much, Susan. As Susan said, the question is what’s happening in PWS research? The answer, of course, is a lot. Today we’ll talk about research updates, including work published with previous FPWR funding, and some of the conferences that took place this fall. Then we’ll spend some time on newly funded projects. Our last grant round brought in more applications than we’ve ever received, and I think we can say with confidence that it also brought in the most strong applications. We tried to fund as many as possible. That leaves us with the good problem of having more grants than we can cover today.

And finally, we'll have time for discussion and questions and answers.

FPWR’s research mission

So, this is just a reminder of our mission, which is to eliminate the challenges of PWS through the advancement of research and therapeutic development. And we do that by building resources and funding projects across the entire research spectrum.

That includes discovery research to understand how the genes in the PWS region work, identifying potential treatment targets, testing them in preclinical models, and moving into clinical trials. We usually support early-stage clinical trials so pharmaceutical companies can take the work forward. Once a therapy or intervention is approved, we try to make sure it’s used as effectively as possible for our families.

Recent publications

So first a word about some of the research that has come out just in the last couple of months from previously funded research. We have been funding research since 2004 and have funded over I think over 300 different projects now. So a lot of work is coming out from the work that we have previously funded. And here's just a selection of them here. We chose these because it really shows the breadth of the funding that we support.

One study looked at how sleep studies are used before infants start growth hormone. Dr. Emily Paprocki and her colleagues surveyed clinicians about whether they obtain sleep studies before babies start growth hormone, which has been a longstanding recommendation. They found that more experienced PWS clinicians sometimes start growth hormone before a sleep study when the baby is doing well and can be monitored closely. That survey, along with other work in the field, is helping inform care guidelines for infants with PWS so they can receive consistently excellent care from the start.

I'll talk a little bit more about this gene therapy paper as well as a paper on siblings. But just to look at some of the other papers, these are pre-clinical studies. So studies understanding the neurobiology of PWS. One is looking at oxytocin receptors and where they are in the brain. So we can understand how oxytocin works in the brain and how it's working differently in PWS.

Another paper from Ryan Butler at UT Southwestern is looking at the electrophysiological properties of neurons in a PWS brain compared to a typical brain. And this is important to understand how the neurons are working potentially differently and also for looking for a way of tracking how the brain cells are behaving in living mice and eventually humans which potentially could serve as a biomarker for the symptoms that we see in PWS.

And finally from Dr. Gallagher's group a look at co-designing a protocol for the development of eye tracking. Dr. Gallagher and her colleagues are looking at eye tracking or how a person with PWS focuses on food visually as a potential measure of their degree of hyperphagia. And this describes a study that they did in how to assess that and they worked closely with caregivers in the field. So that just shows you some of the papers that have been coming out. I'll, as I said, we'll go into a little bit more detail about two of these.

Reactivating silent PWS genes

We have a lot of work going on in genetic therapy. As a reminder, people with PWS lack the usual activity of a set of genes on the paternal copy of chromosome 15. Those genes are normally active only on the chromosome 15 inherited from the father. They’re present on the chromosome 15 inherited from the mother, where they’re usually silent. This is true whether PWS is due to a deletion, uniparental disomy, or an imprinting defect. Much of our work in genetic therapy asks whether we can activate those silent genes on the maternal chromosome.

FPWR is supporting several approaches, including small molecules, gene replacement, CRISPR activation, and the approach in a recently published paper: inhibiting SMCHD1. This work comes from Dr. Marnie Blewitt’s lab. We’ve supported her work through several rounds of funding since 2019. Her

team identified SMCHD1 as a protein that helps silence PWS genes on the maternal copy of chromosome 15. She’s been asking whether blocking that protein could allow those genes to turn on.

Her team published a paper in Science Advances showing that removing SMCHD1 after early development in a PWS mouse model could activate genes on the maternal copy. The mice weighed less in adulthood and had better muscle strength and coordination. This showed that activating those genes had a positive effect in the mouse model.

Because SMCHD1 works elsewhere in the genome, there’s a theoretical concern that inhibiting it could have negative consequences. They didn’t see signs of that in this mouse model, which is encouraging. Dr. Blewitt continues to receive FPWR funding, and her institution has spun out a company, Togglelux Therapeutics, to move the work toward the clinic. We’re excited to see this approach progress alongside the other approaches we’ve funded.

What we’re learning from siblings

I also mentioned a new paper from the FPWR team led by Lauren Schwartz, a clinical psychologist, mom, and FPWR co-founder. She and her daughter Maddie interviewed siblings of people with PWS to understand the challenges they face and what has helped them throughout their lives.

Siblings described emotional and social challenges. They also shared positive experiences. For some, growing up with a sibling with PWS influenced their choice of career. Some also described challenges in their relationship with food, which is worth exploring further.

We asked what helped. Siblings suggested connecting with other siblings of people with PWS and spending time alone with their parents. Some of these findings appear in A Parent’s Guide to Supporting Siblings on the FPWR website. We also held a sibling panel at our last conference, and that’s available on YouTube.

The 2026 FPWR Research Symposium

Okay, so those are some of the recent publications that FPWR has supported. I also mentioned that it's been a busy season for conferences and I'll talk about a couple of those now. Including the FPWR research symposium which was last month in Philadelphia, the NORD breakthrough summit and a research roundup for rare genetic neurodevelopmental disorders.

So first FPWR's 2026 research symposium I thought was a great success. We had participants from seven countries. We gave travel awards to trainees so we could help those young scientists come to the conference where they would be able to interact with others, interact with families and that I think they really appreciated the opportunity to be in person.

We started the conference with something new that we are going to keep because so many of the clinicians and scientists commented that it was their favorite part of conference. We had a family panel talking about what it was like to live day-to-day with PWS. And I think it was really helpful to allow the scientists and clinicians to really understand the impact and the broadness of that impact. Yes, it is hyperphagia, but it's also so many of the other complicated behaviors and medical problems that our kids have. So, that was great. We had about 200 attendees, scientists, basic scientists,

clinicians, pharmaceutical reps. So really across the spectrum and some really robust scientific presentations.

I'll just highlight a few of those. We had several talks on PWS associated behavior. Understanding how the behaviors in PWS is the same and different from some of the behaviors that are in other neurodevelopmental disorders. Also looking at the trajectory, how do these behaviors change over time and how can we intervene to help mitigate some of those behaviors but importantly in a way that is not too much of a burden on families. So that was some of the behavioral talks.

For the first time this year, we saw how very large datasets can help us understand PWS. FPWR supports Dr. Rubenstein and his colleagues at Boston University. They're examining a database that covers more than 300 million people in the United States. They can identify people with PWS and look at complications and medications, which offers insight into care across the country. People often ask how many people in the United States have PWS. The team's estimate was at least 14,000, which I think was higher than some of us expected.

Dr. Sani Roy and her colleagues are using a different data set but also a large data set to look at diabetes and glucose problems in individuals with PWS. So I think this is going to become very common and give us some real insights. And this artwork it was commissioned by Dr. Rubenstein by an artist with PWS as a logo for their project which I thought was very fun.

I know there's a lot of interest in tirzepatide, Ozempic, and other drugs that act on the GLP-1 pathway. One concern is that these drugs can slow the gastrointestinal tract, which may already move more slowly in PWS. Two presentations addressed this. My takeaway was that some of the initial safety findings were less concerning than we might have expected. It's possible there's some slowing, and we need more data to understand how it compares with what we already see in PWS.

And finally just to mention that there is a lot of new drug development. Several posters and presentations looked at different pathways. One of them was based on a drug from oh probably about 10 years ago beloranib which worked very well in PWS but which had side effects sort of building the next generation hoping to get rid of those side effects but keep the efficacy and to look at other pathways that are look like they're disrupted in PWS and may have some drug target. So that is an active area of investigation.

My big picture takeaways from FPWR's conference. We had more clinical presentations than we have had in past years, which was great. There's still a good balance of basic science, discovery science, and clinical care. The molecular studies are informing the studies on drug development. We have a strong pipeline of new drugs and new targets for drug development, which is exciting. The big data I think is going to give us a lot of insight into what care in PWS in the entire population looks like. We saw a lot of excellent young scientists, a lot of vigorous discussion and collaboration going on. It's always good to bring those people bring all the smart people together and just let them talk through the science. I think that is really one of the most important things that FPWR can do. And we heard again and again from the scientists that this work would not be done without the funding that is supported by all of you. So we appreciate that.

Research collaborations

The conference is also a time to gather other groups that are attending conference. The CLIC or the Clinical Investigation Collaborative clinicians got together for a daylong meeting. There are 37 sites across North America that form the CLIC and they collectively care for more than 3,000 PWS patients. So they may these investigators may be taking care of one of your kids. And they are working on a variety of projects to improve clinical care across the entire age spectrum of individuals with PWS. So they were a very dedicated group. They got kind of crunched into a small room and they were troopers about that and worked really hard all day.

We also welcomed the members of the Clinical Trials Consortium. This is a group of pharmaceutical companies academicians and patient advocacy groups all to talk about how do we make clinical trials in PWS more efficient and more effective. So, how do we get to approved drugs more effectively? And we had a great evening meeting. We talked about placebo effect in clinical trials of PWS, which is a real challenge. We talked about the endpoints that we used. And again, a lot of ongoing work with that group.

And finally, we have our scientists that study the MAGEL2 gene, which is one of the genes in the PWS region, lost in PWS and mutated in Schaaf-Yang syndrome. And that group got together again to be coordinating the work that they do so that everybody is more efficient and all of the work gets done faster.

NORD recognition and the Global PWS Registry

Shortly after the FPWR meeting, I was honored to attend the NORD Breakthrough Summit and receive on behalf of FPWR the Abbey S. Meyers Leadership Award. So, NORD awards these rare impact awards once a year and so it was kind of a big deal to get this award, the leadership award. And it was awarded to FPWR, which was great. But really I think it was awarded to our entire community because it was based on the work that we've done using the Global PWS Registry and that work really could not happen without all of us in the PWS community contributing to the data in the Global PWS Registry.

And that data has helped us understand so many things about PWS. We have put many publications into the literature so that any clinician can find that and understand more about strabismus or the neuropsychiatric component of PWS or best practices for feeding tubes for baby with PWS. We've also used it to develop the clinical outcome assessments or the endpoints for clinical trials as a way to validate those. The food safe zone, the PWS profile, the HQ-CT have all been validated in part using the Global PWS Registry. And all obviously to support the clinical trials and in particular the data from the PATH for PWS natural history study from the Global PWS Registry was used to support the approval of VYKAT XR. So all of that was honored by NORD. Our registry platform is on NORD's IAMRARE platform. So they we have worked very closely with them over the years to use the registry in all these ways.

We’re still using the registry in new ways. If your loved one with PWS is taking VYKAT XR, I hope you’ve filled out the VYKAT XR survey so we can learn from your experience. Families have raised some safety concerns, and we want to understand those better. How easy was it to get the

medication? How often did your physician check in while the dose was being adjusted? We presented some of that data at the FPWR conference and are still collecting responses. We want to report on safety and on whether families are seeing benefits, what those benefits are, and how long it takes to see them.

And if you are the parent of a baby or young child age five and under, Dr. Sani Roy and Lynn Bird are working on standards of care for infants with PWS and they want to know about your experience in the hospital. Did you get enough information? How was that information presented to you? If you were unsatisfied with the way that you got information, this is a great opportunity to let Dr. Roy and Dr. Bird know about that because along with their standards of care for physicians, they're going to be developing, how best to communicate to families. What do families need as they're leaving the hospital to be successful and feel, as good as they can getting home and being able to set things up for their newly diagnosed baby with PWS. So, we ask you to please share your baby's experience in the Global PWS Registry.

If you need help, please email us or you can scan this QR code and get an appointment with Lisa who will help you with your record in the registry. So, please reach out to us and we can help you however you need.

Rare disease research and the FDA

Another meeting I attended was the Research Roundup for Rare Genetic Neurodevelopmental Disorders, organized by COMBINEDBrain. PWS is one of thousands of rare genetic neurodevelopmental disorders, and this meeting brought together people working in many of them. Patient advocacy groups, academic medical centers, insurers, pharmaceutical companies, and FDA scientists all attended. It was encouraging to see the FDA there. It’s important to have their input when we’re discussing how to measure the benefits of treatments in clinical trials.

And I will say there was a great discussion about the challenges of these rare neurodevelopmental disorders. These are small populations as we know there's a lot of differences across individuals within the disorder. So PWS manifests very differently across individuals. There's limited clinical expertise. So given all of those challenges, how can we be successful in clinical trials? And I will say that the FDA was extremely engaged. They were thinking creatively along with everyone else in the room about how to get this done. I think they also want treatments to be reaching families but they want them to be effective treatments for sure. So how can we ensure that if a treatment is effective that it's going to kind of show up that way in the data.

So this will be an ongoing discussion. There are plans for another meeting next year, but the focus this time was really on those clinical outcome assessments or the endpoint for clinical trials and how do we generate ones that are robust and can be used to support drug approval. So there will be a report coming out of this which we will share. But it is was a great meeting and really encouraging as far as the FDA really helping this to happen in the rare disease community.

And that is apparent with just a few things that have come out in the last month from the FDA. Probably the most impactful potentially is the new framework for rare disease review for reviewing drugs and biologics in the rare disease space. That's available on FDA's website. They have an open

comment period until December 11th. FPWR will be making a comment. We're going to be emphasizing, for example, that patient advocacy groups and academics really need more formal mechanisms by which to engage with the FDA for things like natural history studies and the development of clinical trial outcome assessments because we're doing that and we don't have the same opportunities that a drug company has to meet with FDA and discuss sort of the technical aspects of those efforts. So if you're interested I think there's a lot going on in the rare disease space at FDA again which is very encouraging.

Clinical trial updates

And speaking of clinical trials I will remind you that there is a lot ongoing in the PWS space and there is more that is about to be developed in the PWS space.

We expect more trials in 2027. The clinical hold on Aardvark Therapeutics' program was lifted, and the company intends to return to clinical trials in 2027. Several companies are enrolling now. Harmony is studying pitolisant for daytime sleepiness in PWS. ConSynance is enrolling for a study of CSTI-500, which is being tested for hyperphagia and behavior in PWS.

There are several other companies that have clinical trials in the planning phase that we expect to see in 2027. So please do keep your eyes or stay aware of that and sign up for our clinical trials alert.

Newly funded research

Okay. So, the awards that we have awarded in this round of funding, as you can see, there's many of them, and I will not go through all of them. I would love to, but we probably don't have until 8:00 tonight. So, we'll pick a few from the general sort of discovery stage. Pick a couple from therapy and target development. So development of drugs and interventions and a couple from the clinical trials and clinical care.

Basic biology and discovery

So first in the area of basic biology and discovery research we're going to look at two studies. The first is from Dr. Giles Yeo who is at Cambridge University who is an expert in the genetics of obesity syndromes including PWS and he and his team have created this amazing resource for the entire scientific community which is a spatial map of the normal hypothalamus. So cell by cell what each cell in the hypothalamus is doing based on what genes it's expressing and where it sits in the hypothalamus. And this is a reference map for understanding the circuitry of behavior and appetite and all the other things that the hypothalamus does which is sort of regulating sleep and food intake, thirst so many things.

Dr. Yeo's team will use the same approach to study donated brain tissue from people with PWS who have died. They'll compare the hypothalamus in PWS with the reference map. This team has a lot of experience studying the genetics and brain circuits involved in eating and obesity. They'll make the resource available to other scientists. That's something we love to support at FPWR because it allows our funding to advance research around the world. The longer-term goal is to identify the circuits affected in PWS and understand which therapies might be most effective.

A second proposal or a second project in the area of discovery and basic biology is looking at the function of the MAGEL2 gene. As I mentioned, MAGEL2 is one of the PWS region genes. It's lost in PWS or not expressed in PWS and it is expressed but mutated in a related disorder Schaaf-Yang syndrome. And [researcher name unclear] has been studying exactly what is MAGEL2 doing and how does that change when it gets mutated and so we know that individuals with Schaaf-Yang syndrome who have the mutated version of MAGEL2 are actually sometimes much more severely affected with respect to cognition and autism compared to individuals with PWS.

And what the researcher's group has found is that the mutated MAGEL2 is actually clumping up and gumming up the cell in a way that is probably causing damage. So in this study she's going to identify sort of the dynamics of that clumping and what MAGEL2 is interacting with and can you add normal MAGEL2 and recover some of that function or is it the fact that the clumped up MAGEL2 is there is that what's causing the problem. So we're excited about this research because it is a experienced researcher. She has done a great job collaborating with others in the field. We funded her initially and she has done some fantastic work with some real molecular insights into MAGEL2's function. They're also making a number of cells that will be available again to all researchers around the globe. So developing resources that can be used by many others.

And the long-term goal of the study is to understand genotype phenotypes. So how changes in the gene result in changes in a whole person in both PWS and Schaaf-Yang syndrome and to understand how mutating MAGEL2 disrupts the cell's function and what proteins are important in that. And she'll also be looking at biomarkers. So proteins that are circulating in the blood that may be able to tell us something about the severity of disease.

Therapy and target development

As I said we have a number of proposals that are looking at the development of new therapies for PWS and this is the preclinical stage. So looking at early on in cells and animal models, usually mouse models of PWS to see if these are going to be viable targets for the future clinical trials.

So one of these is a very interesting gene therapy approach from Dr. Creemers' lab. Dr. Creemers has patients with a different disorder CMS22 and he noticed that they have very similar phenotypes or characteristics to PWS. So in both cases babies are born and they're hypotonic and they have difficulties feeding and then later on they go on to develop obesity and so Dr. Creemers was really intrigued by this similarity and one of the known defects in CMS22 is in mitochondrial function. You'll remember from your high school biology that mitochondria are the powerhouse of the cell. And he found that in CMS22 the mitochondria are defective and he found some of the same similar defects in individuals with PWS or cells from individuals with PWS and mouse models of PWS.

So in this study, he's going to determine whether PREPL, which is the protein that is defective in CMS22, can actually have a beneficial effect in individuals with PWS. And in this case, he's going to be looking at mice with PWS. So this is another this is a second year of funding.

They've been very productive and showing the similarities between CMS22 and PWS. He's collaborating with another FPWR funded researchers [collaborator name unclear] to use these nonviral what we call exosomes to deliver the PREPL gene to mice with PWS. And they'll be doing a

proof of concept study to see whether delivering PREPL to mice with PWS can restore some of the muscle strength and other metabolic aspects that are different in PWS. So the long-term goal of this is to develop a new nonviral gene therapy to activate the PREPL pathway and improve mitochondria metabolism muscle strength in people with PWS.

Another pathway that we're looking at is the PPAR gamma and alpha pathway. And the PPAR is generally a master regulator of fat cell development in organisms. So this pathway is complicated and it is important in where fat cells develop and how big they get. And we know that in PWS even in individuals who are not overweight they do have an unusual distribution of fat cells. They so even in a thin person with PWS there are actually more fat cells than in a typical person who is the same weight. And this is looking at a drug that impacts the PPAR pathways and may change that metabolism.

So this molecule [compound identifier unclear] has been shown in mouse models of obesity. So nonPWS to improve blood glucose levels, reduce fat, maintain muscle mass. So that's important, right? We don't want to necessarily get rid of all of the weight. We want to keep the muscle, lose the fat, and increase energy expenditure.

So Dr. Cao at Ohio State University is going to test this molecule in mouse models of PWS to show whether it is relevant to PWS. So this is a very experienced researcher who we have funded before. She knows how to do these studies very rigorously to get an answer about whether this is something that might be interesting to move into the clinic. The preliminary data is promising and we hope that this project will provide the rationale to move this compound into clinical trials in PWS.

The final grant in this category is from Dr. Svensson, who identified a peptide called BRP. It occurs naturally and has shown appetite-suppressing effects in several species studied outside of PWS. Her team will ask whether it can safely reduce appetite in a PWS mouse model as a first step toward potential human trials. They’ll look at food intake, meal patterns, and whether the peptide can help manage weight over time.

And interestingly we also got another application from [researcher name unclear] who we had supported previously in Dr. Jeffrey Friedman's lab who had done great work in PWS who is also interested in this peptide and Dr. Svensson and her collaborator will be coordinating their work so that they are complementing each other and we can get this peptide evaluated even more quickly.

So we're excited about this study because it addresses an unmet clinical need in PWS a that is the hyperphagia or the appetite in PWS. It's an exciting new compound, a new pathway that's never been explored in PWS. And there was really extensive and rigorous preclinical or preliminary data that the reviewers noted suggested that this would be very well evaluated and, if successful, these studies will move this peptide toward clinical trials and potentially give us a non-GLP option for controlling appetite and weight in PWS.

Clinical research and care

And finally in the area of clinical trials and clinical care I'll mention two studies. The first one is from Dr. Vogel in Germany and he is an expert in proteomics. Looking at proteins and also has expertise in the area of neuroinflammation or he and his team do and they are interested in looking for a non-invasive test so blood or saliva to look at the immune-related changes that may be contributing some to some of the challenges faced by people with PWS.

So there is some evidence that there's neuroinflammation in the brain of individuals with PWS and that could be contributing not only to some of the behavioral issues that we see but also to some of the metabolic disturbances. And so in order to be able to track that and provide the rationale for looking at treatments that reduce neuroinflammation Dr. Vogel is going to be looking and seeing if they can see a signature of changes in the blood in children with PWS.

So this is an experienced group that looks at both PWS and Schaaf-Yang syndrome. They have a lot of experience and proteomics and they as a team have been working on this idea of whether neuroinflammation is underlying some of the major issues in PWS. The ultimate goal of this is to get a biomarker of this neuroinflammation. Which would be great not only for understanding the basis of some of the issues in PWS but also for being able to monitor treatments to see if they actually are reducing neuroinflammation.

And finally Dr. Biaggioni from Vanderbilt Medical Center is an expert in the sympathetic nervous system and he hypothesizes that individuals with PWS have disruptions in the sympathetic nervous system that are responsible for what we see so often this reduced resting energy expenditure. So, we know people with PWS, even if they are on very strict diets and they're not getting many calories each day, they can still put on weight. And so, what is causing that? And he believes that it may be the sympathetic nerve activity is deficient in PWS, but that has never formally been shown using the techniques that he is expert in. And so he'll be looking measuring sympathetic nerve activity and resting energy expenditure in people with PWS and comparing that to people with obesity because of other reasons.

And we're excited about this because there really is very limited understanding of why people with PWS have a decreased resting energy expenditure. And the idea of being able to burn more calories as a potential therapeutic intervention is really attractive. And there are some medications that may be able to stimulate the sympathetic nervous system towards this end, but you have to have the rationale. You have to first show that there really is a deficit here. So, we're excited that this is something that potentially could be translated into a new therapy relatively in a relatively short time frame.

Okay. So, that's all the time I have. There are many other projects that we have also funded. All of them are going to be available on our website. I encourage you to go there and look at the summaries of each of those. We're always the FPWR team is always available to answer any questions you have about that. So it's a really robust round of grants that we're really excited to be funding and again it's all because of the support that we receive from all of you. So very appreciative of that.

Looking ahead to 2027

Looking ahead to 2027, we will be reporting out our experience using whole genome sequencing and precision medicine to better understand the variability we see in symptoms across individuals with PWS and how that might inform clinical care. We'll be advancing these different gene therapies. We talked about SMCHD1 at the beginning of the talk, but there are also the CRISPR approaches and the oral gene therapies that will also potentially be moving forward in pre-clinical development. We're going to see some new clinical trials launching in 2027. So, please keep your eye out for that.

And the FPWR team is really excited that the VNS4PWS study that we've been doing for probably three years now is wrapping up and we'll have our first results on that. So this was using a device, a vagus nerve stimulation device to see if it reduces temper outbursts in people with PWS. And we really appreciate everybody who participated in that trial and we expect to have results coming out probably by the summer.

And finally, we're looking forward to seeing the standards of care for infants with PWS that doctors Roy and Bird are leading and we expect to see that coming out in 2027. So there'll be a lot of really great things again all the way across the spectrum of research and clinical care that we are looking forward to seeing in 2027.

How families can support research

So how can I support PWS research? Please sign up for the registry if you haven't already. If you see one of the physicians in the PWS-CLIC network and that network is on our website. You can see if your physician is part of that. They also have a clinician entered database and hopefully we'll ask you to join that. So please consider that.

You can sign up to hear more about the clinical trials that are coming. We also put opportunities in there for sort of non-drug interventions, behavioral interventions, opportunities to contribute to research in other ways. So, it's not just drugs in clinical trials that are in that clinical trial alert. If you're not able to participate in a clinical trial, please be supportive of people who are because it's only because individuals are willing to participate in clinical trials that we will ever get new medications and devices for individuals with PWS.

And you can volunteer to be an advocate reviewer for FPWR grants. You can contact Caroline at FPWR. And finally, of course, we can't do any of this without the funding that our community brings in. So, if you have the capacity to donate or if you're willing to fund raise, please contact our team.

One last thing. Save the date. Next year, September 24th, 25th, we will have our conference in Houston and hope to see you there.

Questions and answers

Susan Hedstrom. Theresa, thank you so much. That was such an amazing presentation with lots and lots of great information.

There were some questions. One was asking about the sibling workshop and panel from FPWR conference. There was a request for a link to watch those on YouTube. I've put those in the Q&A. So,

I think you all can see the response. There's two links. One is to Dr. Schwartz's presentation. The other is the panel Q&A with three siblings. So, I encourage you all to go check out those links. The content was really quite good.

Theresa, let's answer a few questions submitted through the Q&A. The first is about SMCHD1. You said the protein helps silence the maternal PWS genes, and the goal is to let those genes turn on. What technique would that require? Is it a medication? Is it CRISPR technology? How would you remove or block the protein?

Theresa Strong. Yeah, that's a great question. And in this experiment that was just published, they were doing it with genetic tricks in mice. So you can do genetic manipulation to get rid of that. That would be hard to do in a person. So actually their spinout company is looking at small molecules or drugs that would inhibit the activity of SMCHD1. And that is so potentially like an oral medication that would inhibit SMCHD1's activity. It's a double negative. You're inhibiting the inhibitor which would then allow the PWS genes to be expressed.

You could also look at genetic ways of doing that, but probably the easiest to test in the clinic initially would be a drug to inhibit the activity of SMCHD1.

Susan Hedstrom. Great. I was typing an answer, but I think I'll share the question with the whole group. There was some interest in the VYKAT XR survey and the results like when can we see the results? Would you like to address the time, when can we expect to begin seeing results being pulled from that VYKAT XR survey?

Theresa Strong. We presented early data on how people started VYKAT XR, and the abstracts from the scientific symposium are linked on our website. We looked at how long it took people to get the drug, whether they asked their physician for it or their physician offered it, how often they were monitored, and what insurance covered it. That was plenty for an initial presentation because many people had started the medication recently.

We have not pulled the data on efficacy and safety yet. We wanted to get more data. So we expect to have that data in 2027 and we'll be sharing that data in 2027.

Susan Hedstrom. So yes would it be fair to say that the more people who submit their responses the faster we would be able to share data because we would have more collected.

Theresa Strong. Yes. We don't want to share data on if we have only 10 individuals who have been on it for six months right we wouldn't share that data yet. We want to get enough so that we feel comfortable that it is somewhat representative.

So that's why yeah it would be great if everyone who were on VYKAT XR could enter their data there. Then we could get some real a real sense of what percent of people is it working for? What percent are not seeing any changes? What changes are people seeing and how long is that taking? So really the more data we have on that, the faster we can analyze it and the more confident we can be in the results.

Susan Hedstrom. And we want to hear from people who are currently taking VYKAT XR as well as people who have stopped taking VYKAT XR because those experiences are all important pieces of information.

Who might benefit from genetic therapies?

Susan Hedstrom. All right. Gene therapies. Are these only going to be useful for infants or for children or for adults? What ages are going to receive these gene therapies and who do we think will benefit from them?

Theresa Strong. That's a great question. We don't know the answer yet. More work is underway to see what happens when gene therapy is given to young mice versus adult mice. Those results won't necessarily carry over to humans. We'll learn more when the therapies reach human trials.

Trials will likely start with medically stable young adults or adolescents. Researchers would look for an effect in that group first and then move to younger age groups.

And so one of the big questions to me in the field is what are we going to measure in those individuals and that is a topic of discussion for 2027 in our gene therapy groups. So do we expect hyperphagia to change in an adult? I'm not sure but we'd sure like to test it and there's reason to think that it could. And so I think the answer is going to be that we're just going to have to do it.

We are seeing in other genetic disorders like Rett syndrome that those gene therapies are ongoing. They also started in adults. I don't think there was much expectation that there would be much change in adults, but they actually are seeing some changes in adults. So again it points to the fact that the brain can change even later in life and it is very likely that it will be more effective in young babies and children than it is in older individuals but that's not to say that there won't be some benefit in older individuals.

How has PWS research changed?

Susan Hedstrom. We have several families who are new to the community. Could you give us a sense of how PWS research has changed and how much the field has grown compared with 10 or 20 years ago?

Theresa Strong. Hugely. I would say, 20 years ago anyway, the idea that the brain could change after birth, it was just really scoffed at. And there has been not only work in PWS, but also work in other rare neurogenetic disorders that has shown that you can do interventions even in adults that actually, change the course of the disease.

And in PWS, when my son was born, who is now 32, the general consensus was, well, this is just the way it's going to be. You're never going to be able to treat hyperphagia. It's a change in the hypothalamus. There's nothing to do about it. Well, now we have VYKAT XR. We also have other medications. Beloranib, which I mentioned early, was tested in I think 20 2012 or something like that. So a while ago it was very effective at reducing appetite and that was the first indication that even in adults you can change the appetite and up until that point as I said the general consensus was that

there's nothing to be done about that. So that has sparked a whole lot of interest in different medications that regulate appetite.

The other thing that we've seen is in general obesity, of course, nothing worked for years and years and years. And now with the GLP-1 drugs, that is effective in many cases of obesity. It does not appear to be as effective in individuals with PWS, but there are new versions of those GLP-1 drugs and multiple that target multiple things that may be more effective in PWS. So, the general obesity field has changed. Neuro developmental the understanding of neurodevelopmental disorders and the as we say the plasticity of the brain which is the ability of the brain to change has changed and all of those things have led to a lot more research

And then honestly FPWR has really worked hard to bring more researchers into the field and we've been really successful about at it and so we have scientists now that we've supported who come from general obesity who come from neurobiology who come from genetics and now are all working on PWS and the breadth and number of scientists is really different even from 10 years ago in the PWS field and the quality of proposals that we're seeing has really improved over the years as well. Not that the early ones were not the early ones were good but there were less of them and now we have tons of really good proposals.

Susan Hedstrom. Yeah, it seems like 10 years ago there weren't very many clinical trials. I don't recall them until beloranib and since then there's now at any given time three to six clinical trials enrolling with multiples in the wings preparing. And now with this first, approved drug for treatment, I'm really optimistic that we're going to begin to see it more treatments coming through the pipeline and getting approved. What's your take on that?

Theresa Strong. Yes. I think VYKAT XR has paved the way. It has been a game changer for many families. Like any drug, responses vary, so having options will be important. I think this is the start of developing more treatments for people with PWS.

Closing

Susan Hedstrom. Absolutely. So what I what I'm seeing here is we have a lot of momentum. A lot of great work is happening and it's all happening because of the engagement of our community. Truly all the work that's able to be done that Theresa has shared today has been because families like those who are attending today have fundraised, donated, and participated in clinical trials. So thank you to everyone for that. We are at the top of the hour. This webinar has been recorded. We will make it available soon. And thank you to all for having shared on this important update. Have a great day. Bye-bye.